

Applicants had previously submitted a Declaration of Todd M. Boyce pursuant to 37 C.F.R. § 1.131 (the "Boyce Declaration") to antedate Boyce et al. However, in the April 2 Office Action the Examiner asserted the Boyce Declaration was deficient because it was not submitted by all of the inventors and did not sufficiently establish that Claim 1 was within the scope of the invention shown in the declaration.

By way of antedating Boyce et al. applicants submit herewith a Combined Declaration of Todd M. Boyce and Albert Manrique (the inventors herein) under 37 C.F.R. § 1.131 (the "Combined Declaration"). As set forth in the Combined Declaration, Boyce et al. issued on May 4, 1999 on original application Serial No. 09/009,997 filed on January 21, 1998. The subject application was filed on April 5, 2000 as a continuation of U.S. patent application Serial No. 09/020,205 filed February 6, 1998.

As detailed in the Combined Declaration, especially Example 2 of Exhibit A to the Combined Declaration, a solid aggregate, i.e., a pellet, was made of demineralized elongate bone fibers in which individual demineralized bone fibers were bonded to each other through chemical linkages between their surface-exposed collagen. The pellet of Example 2 of Exhibit A was produced by demineralizing bone followed by its placement "in polyethylene glycol diglycidal ether for 12 hours at room temperature." As set forth on page 3 of Exhibit A, "chemicals which act as collagen cross-linkers include: ...polyepoxy compounds such as...polyethylene glycol diglycidal ethers...." This clearly encompasses the solid aggregate of Claim 1 wherein the demineralized bone-derived elements are bonded to each other through chemical linkages between their surface-exposed collagen. As such, the pellet of Example 2 of Exhibit A is an

embodiment of Claim 1 of the subject application. (See MPEP § 715.02 (reference applied against generic claims may be antedated by an affidavit or declaration pursuant to 37 CFR § 1.131 showing completion of the invention of only a single species within the genus prior to the effective date of the reference.)

Moreover, Examples 1, 3, 4, and 5 of Exhibit A combine multiple layers of sheets (Examples 1, 4 and 5) or bone cubes in combination with bone slices (Example 3). Cross-linking of surface exposed collagen takes place by placing the demineralized bone into 10% neutral buffered formalin (Examples 1, 3 and 5) or by treating the bone with transglutaminase (Example 4). As all of these examples encompass cross-linking of multiple layers or pieces of bone through their surface exposed collagen, applicants respectfully submit the resulting implant would encompass the solid aggregate of Claim 1 or, in the alternative, be obvious to one skilled in the art reviewing Exhibit A.

Accordingly, Claims 1-7, 9-21, 23-43, 45-61, 63-80 and 82-134 are not anticipated by Boyce et al. Moreover, as Claims 95-134 were rejected on no ground other than on anticipation over Boyce et al., applicants respectfully submit that Claims 95-134 are in condition for immediate allowance, formal notice thereof by the Examiner being respectfully requested.

The Examiner has made final the rejection of Claims 1-7, 9-11, 13, 14, 19-21, 23, 24, 34-43, 45, 56-61, 63, 74-80, 82 and 93-94 under 35 U.S.C. §102(b) as anticipated by Lyle U.S. Patent No. 5,061,286 ("Lyle"). According to the Examiner, Lyle discloses demineralized bone particles that are "linked together" with a binder such as cyanoacrylate. The Examiner asserts: "that the adhesives or binders inherently act via covalent or non-covalent bonds. Even if the adhesives or binders

were said not to act through covalent bonds, since adhesives and binders of Lyle can act via hydrogen bonding, Van der Waals bonds, ionic bonds, and other non-covalent bonds, the Examiner posits that the present claims are inherently met in this regard." (April 2, 2003 Office Action at page 2.)

The Examiner's position ignores the fact that while the Lyle demineralized bone particles possess surface-exposed collagen, there is not the slightest hint anywhere in this disclosure of the demineralized bone particles being "bonded to each other through chemical linkages *between their surface-exposed collagen*", as is clearly required by Claim 1. Contrary to the Examiner's assertion, Lyle's cement or adhesive component does not form or provide *chemical linkages* between the surface-exposed collagen of adjacent bone-derived elements as in the osteoimplant of applicants' claims but applies demineralized bone particles to the surface of a prosthetic device by means of a material that functions as an adhesive or cement, specifically, a cyanoacrylate. As previously noted by applicants, cyanoacrylates work as adhesives by curing, which is to say, polymerization, to form a polymer. Cyanoacrylates provide chemical bonds but those bonds are formed between monomeric units of cyanoacrylate to provide the polymeric adhesive. The chemical bonds that form during the curing of the cyanoacrylate do *not* form between surface exposed collagen of the Lyle demineralized bone particles but, as said, between units of cyanoacrylate monomer. There is nothing in Lyle or in the literature of cyanoacrylate adhesives to indicate otherwise.

One skilled in the art reviewing Lyle would clearly recognize that cyanoacrylate adhesives as disclosed therein differ from applicants' claimed invention wherein

individual bone elements are "bonded to each other through chemical linkages between their surface-exposed collagen". In lacking any disclosure or suggestion of such chemical linkages, Lyle fails to anticipate or render obvious the subject matter of any of Claims 1-7, 9-11, 13, 14, 19-21, 23, 24, 34-43, 45, 56-61, 63, 74-80, 82 and 93-94.

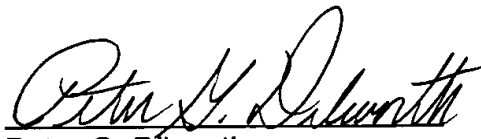
The Examiner has made final the rejection of Claims 12 and 15-18 under 35 U.S.C. §103(a) for obviousness over Lyle. The Examiner characterizes Lyle's "cyanoacrylate" as a crosslinking agent. However, as noted above in connection with the Examiner's rejection of the claims for supposed anticipation by Lyle, cyanoacrylate is a monomer which provides a polymer, the polymer being the actual adhesive which binds the Lyle demineralized bone particles together. There is no disclosure or suggestion in Lyle that cyanoacrylate functions in any other way.

In the absence of any indication in Lyle that the demineralized bone particles therein are bonded to each other through chemical bonds formed in their collagen-exposed surfaces, Claims 12 and 15-18 can only be regarded as nonobvious, and therefore patentable, over Lyle.

In view of the foregoing remarks, reconsideration and allowance of all the claims of the application, i.e. Claims 1-7, 9-21, 23-43, 45-61, 63-80 and 82-134, are respectfully requested.

Respectfully submitted,

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